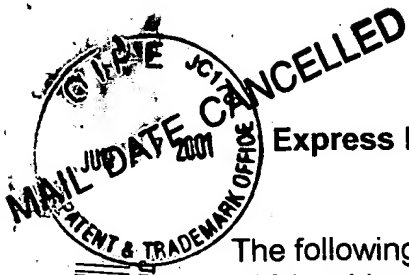


06-27-01

JG04 Rec'd PCT/PTO 25 JUN 2001 PCT



**Express Mail Certificat for Amendment Response to Office Action for
Application No. 09/623, 068.**

The following items have been deposited with US Express Mail today June 25, 2001, addressed to the Commissioner of Patents and Trademarks, Washington, DC 20231. Express Mail Label.

ET 643650659 US

- 1) Amendment/Response 8 pages
- 2) List of Acronyms used in genome research 14 pages.
- 3) Copy of Transmittal Letter to the United States Designated/Elected Office (DO/EO/US) Concerning a filing under 35 USC 371, filed with PCT/US99/04376 (matured into US National Stage application No. 09/623, 068) on 8/26/2000 on Entry into US National Stage. 2 pages
- 4) Copy of Letter requesting Amendments to PCT Application PCT/US99/04376 upon 30 month entry into US National Stage. (2 pages)
- 5) Two return receipt post cards.

Deposited by me with US Mail today, June 25, 2001.

Robert McGinnis

Robert McGinnis, Registration No. 44,232

TRANSMITTED LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER

INTERNATIONAL APPLICATION NO.
PCT/US99/04376

INTERNATIONAL FILING DATE
26 February 1999

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)

PRIORITY DATE CLAIMED
26 February 1998

TITLE OF INVENTION
TWO-DIMENSIONAL LINKAGE STUDY TECHNIQUES

APPLICANT(S) FOR DO/EO/US
MCGINNIS, Ralph, Evan MCGINNIS, Robert Owen

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ has been transmitted by the International Bureau.
 - c. ☒ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☒ have been transmitted by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☐ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☐ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A substitute specification.
16. ☒ A change of power of attorney and/or address letter.
16. ☒ Other items or information:

Two signed small entity statements. A signed letter (2 pages long) requesting amendments. 7 Replacement pages, each replacement page with header "PCT/US99/04376(U.S.National Stage Entry Aug. 2000)". Replacement pages are as follows: background replacement page number 5, background replacement page number 6, background replacement page number 7, background replacement page number 8, specification replacement page number 38, specification replacement page number 43, specification replacement page number 46. Express Mail Mailing Certificate, Return Receipt Postcard, Cenwest check for \$48 (small entity Basic National Fee). Statement under Article 19(1).

Copy filed Aug 26, 2000

7. ☒ The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):

Neither international preliminary examination fee (37 CFR 1.482)
nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO
and International Search Report not prepared by the EPO or JPO \$970.00

International preliminary examination fee (37 CFR 1.482) not paid to
USPTO but International Search Report prepared by the EPO or JPO \$840.00

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but
international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$690.00

International preliminary examination fee paid to USPTO (37 CFR 1.482)
but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$670.00

International preliminary examination fee paid to USPTO (37 CFR 1.482)
and all claims satisfied provisions of PCT Article 33(1)-(4) \$96.00

ENTER APPROPRIATE BASIC FEE AMOUNT =

\$ 96.00

Surcharge of \$130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30
months from the earliest claimed priority date (37 CFR 1.492(e)).

\$

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE
Total claims	20 - 20 =	0	X \$18.00
Independent claims	3 - 3 =	0	X \$78.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ \$260.00

\$

\$

\$

TOTAL OF ABOVE CALCULATIONS =

\$ 96.00

Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement
must also be filed (Note 37 CFR 1.9, 1.27, 1.28).

\$

48.00

SUBTOTAL =

\$ 48.00

Processing fee of \$130.00 for furnishing the English translation later than ☐ 20 ☐ 30
months from the earliest claimed priority date (37 CFR 1.492(f)).

\$

TOTAL NATIONAL FEE =

\$ 48.00

Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be
accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property

\$

TOTAL FEES ENCLOSED =

\$ 48.00

Amount to be
refunded:

\$

charged:

\$ 48.00

a. ☒ A check in the amount of \$ 48.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees.
A duplicate copy of this sheet is enclosed.

c. ☐ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any
overpayment to Deposit Account No. _____. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Robert Owen McGinnis
1575 West Kagy Blvd.
Bozeman, Montana 59715

SIGNATURE:

Robert O. McGinnis

NAME:

44, 232

REGISTRATION NUMBER

1/2 Letter requesting Amendments to PCT Application PCT/US99/04376 upon 30 month entry into the U.S. National Stage (August 26, 2000)"

1 (The amendments do not add new matter to the specification. Claims are being cancelled.)

2
3 The applicants hereby request the following amendments to the application upon entry into the
4 U.S. National Stage:

5
6 Amendments to the background of the application:

7 1) page 5 line 22 after "territory" insert --and that it was difficult to predict the power of using a
8 less dense map at that time--

9 2) page 5 line 22 after "¹⁰" insert -- The inventor's work, however, is a predictor of the power
10 and success of a less dense map.--

11 A replacement page 5 with header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is
12 enclosed to effect these amendments 1) and 2) to the background.

13 3) page 6 line 22 after "TDT," change the text "**to increase the likelihood of conditions**
14 **occurring that increase the power of the TDT in the linkage study, the bi-allelic markers**
15 **used in the study are chosen so that the least common allele frequencies of the markers**
16 **vary systematically over a range or subrange of least common allele frequency.**" from bold
17 face italics to regular italics with underlining. A replacement page 6 with header
18 "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is enclosed to effect amendment 3) to
19 the background.

20 4) page 7 line 6 after "TDT," change the text "**to increase the likelihood of both criteria (1) and**
21 **(2) occurring for one or more markers, so as to increase the power of the TDT in the**
22 **linkage study, the bi-allelic markers used in the study are chosen so that the least**
23 **common allele frequencies of the markers vary systematically over a range or subrange of**
24 **least common allele frequency AND the chromosomal location of the markers vary**
25 **systematically over one or more chromosomes or chromosomal regions. And the bi-allelic**
26 **markers are chosen so that the markers' chromosomal locations and least common allele**
27 **frequencies vary systematically in an essentially independent manner.**" from bold face italics
28 to regular italics with underlining.

29 5) page 7 line 32 delete the text in brackets [*In addition, the two-dimensional linkage study*
30 *techniques do not necessarily favor using markers in a scan that are about evenly spaced*
31 *along a chromosome as in the conventional techniques. This is because*]. On page 7 line 31
32 after the text "unfavorably" insert on the insert --Conventional techniques use a one-
33 dimensional concept of "closeness". *These techniques space markers about evenly along*
34 *a chromosome in the hope that some markers will be "close" (on the chromosome) to the*
35 *sought gene. (They also favor bi-allelic markers with least common allele frequencies near*
36 *0.5.) These--.*

37 A replacement page 7 with header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is
38 enclosed to effect amendments 4) and 5) to the background.

39 6) page 8 line 18 insert on the next line after "background" -- Summary

40 **Versions of the invention use a new, two-dimensional concept of "closeness" for**
41 **association-based linkage studies. Versions of the invention use bi-allelic markers that "cover"**
42 **or are distributed approximately evenly (or systematically) over two-dimensional regions. These**
43 **regions have the two dimensions of chromosomal location and least common allele frequency.**
44 **Conventional techniques suffer from a kind of one-dimensional lack of depth perception.**
45 **(They also favor bi-allelic markers with least common allele frequencies near 0.5.) Two-**
46 **dimensional linkage study techniques overcome this lack of depth perception. These two-**
47 **dimensional techniques greatly increase the chance that one or more markers used in a study will**
48 **be close to the sought gene in two-dimensions. This results in more powerful, systematic and**
49 **efficient methods (including computer programs) and machines for finding genes, such as harmful**

Copy filed Aug 26, 2000
Cm

2/2 Letter requesting Amendments to PCT Application PCT/US99/04376 upon 30 month entry into the U.S. National Stage (August 26, 2000)"

1 genes and genes of only modest effect. These techniques also use less dense (more efficient)
2 marker maps (or marker "coverings").
3 The basic principles behind the two-dimensional approach spawn numerous other inventions.
4 These include methods, machines and compositions of matter (groups of molecules) used for
5 gathering the data (i.e. genotype/sample allele frequency data) used in the new two-dimensional
6 studies, and computer techniques for using and handling such data. These techniques work for
7 creatures other than human beings. And they work for markers and genes that are not bi-allelic
8 (any marker or gene can be mathematically transformed to behave like it is bi-allelic). This
9 summary is not exhaustive or limiting, there are other inventions not listed or specifically
10 described here.--

11 A replacement page 8 with header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is
12 enclosed to effect amendment 6) to the background.
13

14 Amendments to the Description

15 7) page 38 line 2, page 38 line 17 and page 38 line line 20 delete the text "Best Mode" and
16 replace the text "Best Mode" with the text "Set/Subset Example". A replacement page 38 with
17 header "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is enclosed to effect the
18 amendments to the description under item 7).

19 8) page 43 line 4 delete the text "Best Mode" and replace the text "Best Mode" with the text
20 "Set/Subset Example". A replacement page 43 with header "PCT/US99/04376(U.S. National
21 Stage Entry Aug. 2000)" is enclosed to effect the amendment to the description under item 8).


22 9) page 46 line 24 and line 28 delete the text "Best Mode" and replace the text "Best Mode" with
23 the text "Set/Subset Example". One page 46 lines 26 and 27 delete the text "Best Mode" and
24 replace the text "Best Mode" with the text "Set/Subset". A replacement page 46 with header
25 "PCT/US99/04376(U.S. National Stage Entry Aug. 2000)" is enclosed to effect the amendments
26 to the description under item 9).
27

28 Canceling of Claims and presentation of uncanceled claims for examination

29 The applicants hereby request that all claims in the application be cancelled except for the
30 following claims that were filed April 17, 2000: Claims 3, 4, 5, 7, 8, 20, 21, 22, 23, 33, 34, 35, 37,
31 38, 50, 51, 52, 53, 54, 57. Thus the applicants request that only claims 3, 4, 5, 7, 8, 20, 21, 22,
32 23, 33, 34, 35, 37, 38, 50, 51, 52, 53, 54, 57 filed April 17 2000 be examined.
33

34 I hereby attest that no new matter is added to the specification of the application by the
35 amendments requested in the two pages of this letter.
36

37 Respectfully submitted,

38 

39 Robert McGinnis
40 U.S. Patent Agent 44, 232
41
42

*Copy filed
Aug 26, 2000*